"The Electromotive Phenomena in Mammalian Non-medullated Nerve."

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(From the Physiological Laboratory of the University of London.)

Up to the present time there would appear to have been no published researches on isolated mammalian non-medullated nerve, and indeed, except for the paper of Brodie and Halliburton,* all our knowledge of these nerves has been either by inference from similar nerves in cold-blooded animals or derived incidentally from experiments undertaken for a different object.

When it appeared, therefore, that the technique for mammalian medullated nerve served equally well for the non-medullated,† it became a matter of interest to examine the phenomena displayed by the latter, and the very evident advantages of dealing with nerves of considerable size and comparative longevity, and the possession of a ready standard of comparison in the medullated nerves of the same animal, greatly assisted in obtaining an exact result.

Methods.

The splenic nerves were found to be very suitable objects for this purpose. They consist almost entirely of non-medullated fibres,‡ and in the horse, which is the animal which has been used for these experiments, the various bundles form a plexus around the splenic artery, which can be separated by careful dissection into its component parts, giving isolated pieces of nerve 1—1·5 mm. in diameter and from 6—8 cm. in length. These pieces will commonly retain their irritability for several hours if kept in 1·05 per cent. salt solution at 18° C., into which they are placed from a quarter to half an hour after the death of the animal. Waller's§ galvanographic method was employed as well as the capillary electrometer.||

In the experiments on the negative variation, the exciting current was derived from an accumulator of large capacity, in order to secure the greatest possible constancy, and the excitation was maximal, except in Experiment 716. The temperature at which the experiments were

* Brodie and Halliburton, 'Journ. of Physiol.,' vol. 28, p. 181.

† 'Roy. Soc. Proc.,' February, 1902, p. 264.

‡ The proportion of non-medullated to medullated fibres varies in different animals; sections made from the nerves actually used showed that medullated fibres formed less than 0·5 per cent. of the total number.

§ Waller, "Signs of Life," 1903.

|| The analysis of the electrometer records will be considered at a future time.

conducted was 17—19° C., except where otherwise stated. The current of injury was balanced against an equal fraction of a volt, and the value read off. This compensation was maintained throughout the experiment. No current, therefore, flowed through the nerve when at rest.

The experiments were ordinarily carried out in duplicate, with both medullated and non-medullated nerves from the same animal.

The electromotive phenomena are considered in the present paper under two heads:—

1. Negative variation.
2. Electrotonic currents.

1. Negative Variation.

(*Experiments.*)

The electromotive phenomena in the nerves of the horse resemble those in the nerves of other mammalia in kind, but differ in degree, being of considerably less magnitude.* This is due, in part, to the large amount of connective tissue surrounding the nerves, and forming a derivation circuit. When this connective tissue is dissected off, the effect on the galvanometer is increased. Three experiments may be quoted on this point:—

Table I.

Experiment.	Nerve.	Current of injury.	Negative variation.	Notes.
		millivolts.	millivolts.	
720 (A) *a*...	Median	2·7	0·172	
720 (A) *b*...	,,	4·1	0·309	
747 *a*......	,,	8·2	0·242	
747 *b*......	,,	8·5	0·359	
749 *a*......	Splenic	9·7	0·504	Whole nerve.
749 *b*......	,,	11·3	1·910	Single nerve-bundle.

The nerve was isolated in the usual way and the measurements made that are marked *a*, the connective tissue was then dissected off as far as possible, and the measurements *b* taken. Both injury current and negative variation are increased, the latter more than the former. But it will be noticed that even in the most favourable case the voltage of the negative variation is less in the medullated nerves of the horse

* This has already been observed in the case of the current of injury, see Gotch, 'Schäfer's Text-book,' vol. 2, p. 520, and Biedermann, 'Elektrophysiologie,' 1895, p. 638.

than is usual in the mammalia. It is not certain how far this is due to the greater amount of connective tissue present between the individual nerve-fibres, or to some other cause.

Both current of injury and negative variation are considerably greater in the non-medullated nerves of the horse than in the medullated. The following table gives the result of several observations :—

Table II.

Nerve.	Current of injury.*		No. of experiments.	Negative variation.*		No. of experiments.
	Mean.	Max.		Mean.	Max.	
Median	3·86	5·3	5	0·380	0·83	4
Splenic	5·81	15·5	13	0·860	2·3	11

These are the values obtained with the galvanometer. They are probably too low, and for several reasons it is likely that the maximum values are more nearly correct than the mean. They are, however, strictly comparative, and it is seen the voltages in the splenic nerves are approximately three times the median, a result agreeing with the observations on cold-blooded animals.† The non-medullated nerves of

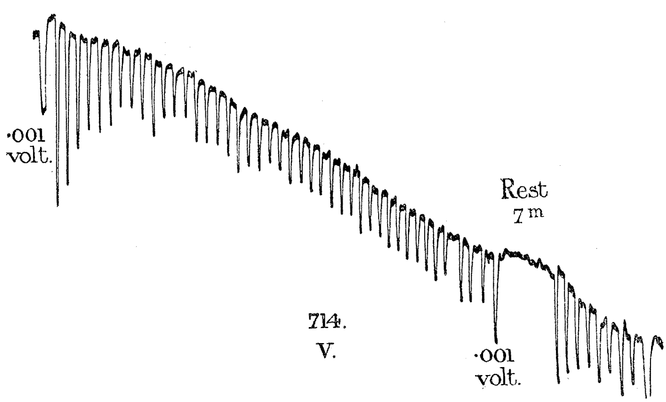

FIG. 1 (Exp. 714, V.).—Splenic of Horse. The vertical lines are the successive negative variations produced by tetanising currents (5000 Berne units, 2 volts in primary circuit) for 13 seconds, repeated once a minute.

* Here and elsewhere in millivolts.

† Kühne u. Steiner, 'Unters. d. Physiol. Inst. d. Univ. Heidelberg,' vol. 3, p. 149 ; Sowton, 'Roy. Soc. Proc.,' vol. 66, p. 379.

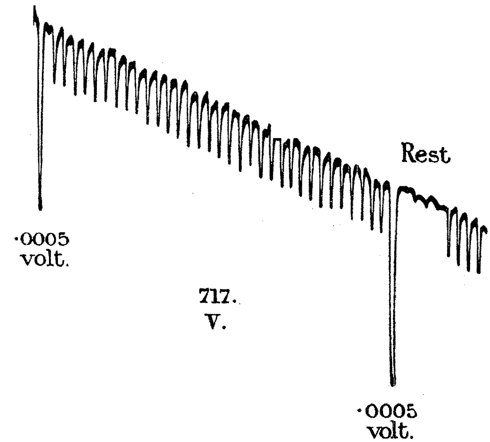

FIG. 2 (Exp. 717, V.).—Median of same animal as Fig. 1. All details as before.

the horse commonly retain their excitability for 8—10 hours *post-mortem*, the medullated for about half this time.

I have been unable so far to trace any quantitative relation between the current of injury and the negative variation as determined above.

Obtaining a non-medullated nerve, subjecting it to a series of repeated tetanisations, and recording the successive negative variations by the galvanographic method, it appears at once that the results are very different from the corresponding phenomena in medullated nerve. Figs. 1 and 2 are records from two nerves, the one splenic and the other median, from the same animal under identical conditions. The successive negative variations from the latter are approximately equal, those from the former fall off very rapidly, and this rapid decrease in the negative variation is characteristic of mammalian non-medullated nerve. The following experiments were made:—

Table III.—Splenic Nerves.

Experiment.	Neg. var. = a. Initial.	Neg. var. = b. Final.	Duration of experiment.	Diminution b/a.	Notes.
	millivolts.	millivolts.	mins.		
702. Horse I	0·95	0·33	11	0·35	Exc. lasting 10 seconds, once a minute.
704. ,, I	0·376 (1st) 0·397 (2nd)	0·219	25	0·582	Same nerve as Exp. 702.
705. ,, II	0·491 (1st) 0·576 (2nd)	0·109	22	0·222	
707. ,, III	0·317	0·131	26	0·413	
709. ,, III	0·560	0·396	30	0·710	
712. ,, IV	0·788 (1st) 0·847 (2nd) 0·878 (3rd) 0·792 (4th)	0·672 (23rd)	23	0·853	Same nerve as in Exp. 710 below, "staircase."
713. ,, IV	0·859	0·392	29	0·456	Same nerve as Exp. 710.
716. ,, V	0·593 (1st) 0·729 (2nd) 0·663 (3rd) 0·607 (4th)	0·215	50	0·362	Submaximal excitation, 500 units, "staircase."
Mean of eight experiments	0·617	0·307	27	0·498	

The following experiments were made under identical conditions with medullated and non-medullated nerves from the same animal:—

Table IV.

Experiment.	Nerve.	Neg. var. Initial = a.	Neg. var. Final = b.	Duration of experiment.	Diminution, b/a.	Notes.
710. Horse IV	Splenic	0·884 (1st) 1·020 (2nd) 0·951 (3rd)	0·600	31	0·679	"Staircase."
711. "	Median	0·219 (1st) 0·233 (2nd)	0·241	31	1·10	"
714. Horse VI	Splenic	2·32	0 636 (33rd) 0·593 (42nd)	33 42	0·274 (0·256)	The bracketed figures refer to the continuation of the experiment beyond the comparison point (figs. 1 and 2).
717. "	Median	0·154	0·125	33	0·812	
720, B. Horse VII	Median	0·292	0·294	22	1·01	For the analysis of the latter portion of the experiments see Table V.
721. "	Splenic	1 60	0·500 (22nd) (0·372) (52nd)	22 52	0·313 (0·233)	
Mean of Expts. 710, 714, 721	Splenic	1·601	0·579	29	0·382	
Mean of Expts. 711, 717, 720, B.	Median	0·222	0·220	29	0·991	

These tables show very clearly the alteration in the negative variation by successive excitations. The decrease is most rapid at first, and after a little proceeds quite slowly, especially if the excitation is sub-maximal, so that if the result of the first few minutes is discarded, there remains a considerable period during which the diminution is small, and which can be used to test any desired procedure (*vide* figs. 1 and 6). The effect of rest is that the subsequent responses are greater for a time, but soon fall off (fig. 1), and the difference in this respect from the medullated nerves is very marked (fig. 2); in the latter the subsequent negative variations are almost invariably less after a pause.

This difference is very clearly seen in the electrometer photographs (Experiment 750, B, fig. 3, splenic of horse, and Experiment 751, fig. 4,

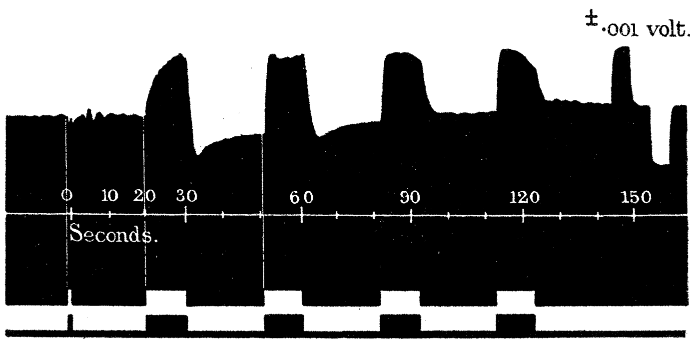

FIG. 3 (Exp. 750, B,).—Non-medullated Nerve, Splenic of Horse. Excitation for 10 seconds (Tet.), interval 20 seconds, as shown by the lower interrupted line.

Time—1 mm. = 2 seconds.

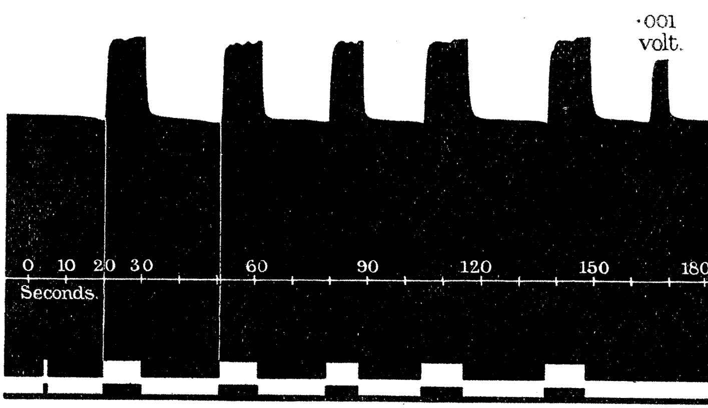

FIG. 4 (Exp. 751).—Medullated Nerve, Ulnar of Cat. Details as in Fig. 3.

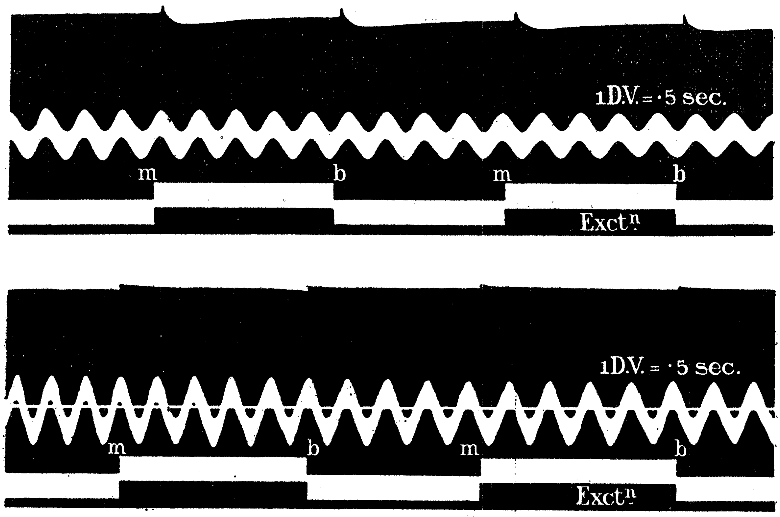

FIG. 5 (Exps. 750 B and 751).—Response of Non-medullated Nerve (upper) and Medullated (lower) to Single Shocks. Same nerves as figs. 3 and 4.

ulnar of cat). The full analysis of these will be considered in a subsequent paper, but these figures show (*inter alia*) that the electrical resistance plays an unimportant part in the production of the phenomena observed, and that the rate of transmission of the electrical effect is very much less in the non-medullated nerves.

As, therefore, the progressive diminution in the negative variation is characteristic of non-medullated nerve, both here and in cold-blooded animals,* further experiments were undertaken to ascertain whether this was due to events occurring along the whole length of the nerve, or to changes localised at the place of excitation. Two pairs of platinum wire electrodes were used for stimulation, placed respectively further and nearer the leading-off electrodes; the nerve was excited first at the "far" pair and then at the "near."

In Experiment 718 (fig. 6) the result of exciting through the near pair of electrodes was to increase the negative variation to very nearly the original amount (*a*). After 12 minutes of excitation at this point the current was again sent through the "far" electrodes, and the resultive negative variation (*c*) was much less than the original value. If the nerve had been simply resting, instead of being excited at a proximal place, the negative variation would have been increased (see fig. 1); *the effect, therefore, of passing a recently excited spot is diminution.*

In Experiment 719 the excitation was through three pairs of

* Sowton, *loc. cit.*

Table V.

Experiment.	Far. Negative variation. Initial.	Far. Negative variation. Final.	Far. Time.	Near. Negative var. Initial.	Near. Negative var. Final.	Near. Time.	Notes (see below).
			min.			min.	
716. Horse VI	*a* 0·694 (1st) 0·839 (2nd)	0·419	29	*b* 0·800	0·372	12	Fig. 6. *a* = far. *b* = near. *c* = far again.
	c 0·166	0·20	6				
719. ,, VI	*a* 0·111 (1st) 0·144 (2nd)	0·1109	24	*b* 0·400 *c* 0·322 *c** 0·092	0·138 0·092 0·115	18 14 3	*a* = 1st pair. *b* = 2nd pair. *c* = 3rd pair. *c** = 3rd pair reversed.
721. ,, VII	*a* 1·60	0·372 (0·496)	52 (17)	*b* 1·22	0·764	17	
720, B. ,, VII	*a* 0·292 *c* 0·253	0·294 0·281	22 5	*b* 0·355	0·378	20	Control with medullated nerve. *a* = far. *b* = near. *c* = far again.

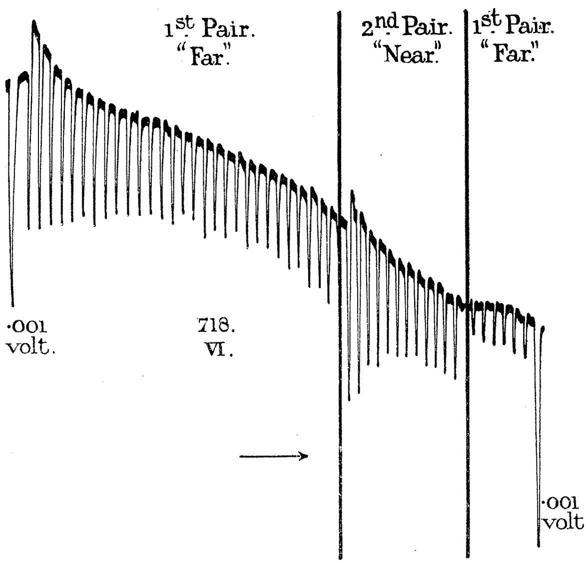

FIG. 6.—Splenic of Horse. Negative Variations. Result of exciting at (1) far, (2) near, and (3) far electrodes.

electrodes, and then the excitation was reversed; the alteration produced by reversal was very small.

Experiments 721 and 720 were with non-medullated and medullated nerves under the same conditions.

Considering the result of all these experiments, it is clear that the diminution of the negative variation in non-medullated nerves is due to changes occurring at the point where the nerve is excited. Using a constant stimulus this spot becomes less and less excitable, in the sense that the response becomes progressively smaller. The control experiments on medullated nerve show but slight traces of this effect,* either the medullary sheath prevents this loss of excitability in some way, or the two classes of nerves differ very widely in their reaction to stimuli. Speaking broadly, the evidence is in favour of the former hypothesis.

While the work of Sowton† and Garten‡ on cold-blooded nerves is in accord with my results on mammalian nerve, the paper of Brodie and Halliburton at first sight offers a contradiction. These experimenters excited the splenic nerves in the dog for many hours, and blocking the impulse by cold, observed that when the block was removed the splenic contractions followed as at first, apparently unaltered in amount. I have no doubt as to the correctness of their observations, and the results they obtained, differing from those

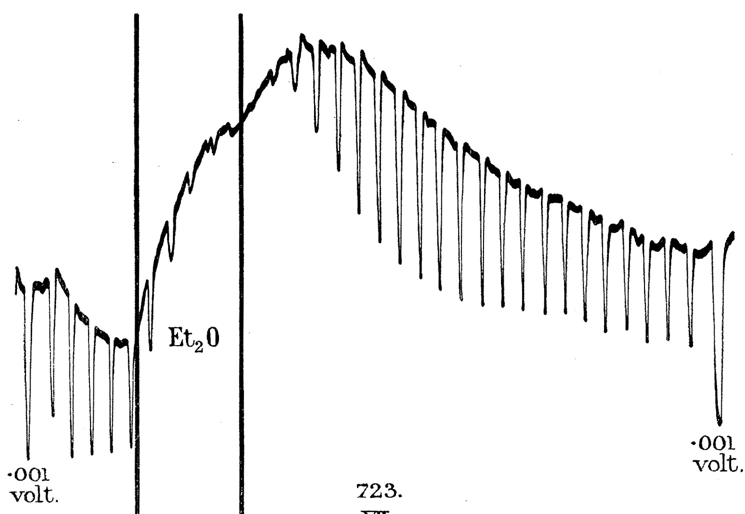

FIG. 7.—Splenic of Horse. Effect of Ether Vapour.

* Dr. Waller has very kindly permitted me to measure a considerable number of his photographic records of frog's nerve, of 1896—1897; in all a small regular diminution is detectable, amounting to from 2·0 to 5·6 per cent., in experiments lasting 40 minutes.

† Sowton, *loc. cit.*

‡ Garten.

recorded above, may possibly be explained by supposing that the splenic contractions are not as delicate an index of the condition of the splenic nerves as the galvanometric response. Waller* has shown that with a gradually increasing stimulus the voltage of the negative variation reaches its maximum much later than the contraction of the attached muscle, and as in all the experiments here recorded a certain amount of the negative variation still persisted, it is possible that even this fraction—perhaps one-third of the initial value—indicated a sufficient intensity of nerve impulse to give a maximal splenic contraction.

If the medullary sheath has any such action as the hypothesis suggested above necessitates, the inquiry may be extended to see if any light can be thrown on the manner in which this sheath acts. The following experiments on electrotonic currents were, therefore, undertaken.

2. Electrotonic Currents.

Methods.

The nerve rested upon two pairs of non-polarisable electrodes. The distal pair led off to the galvanometer; the proximal were connected with the automatic reverser, used by Dr. Waller in 1897, which delivered in order—

(1) A current in the proximal direction (giving anèlectrotonic currents in the nerve).

(2) Excitation by means of an induction coil.

(3) A current in the distal direction (katelectrotonic currents).

(4) Excitation as No. 2.

The result is seen in the photographic plate as a cycle consisting of one upward mark, anelectrotonus, and three downward, the middle one katelectrotonus, the two side negative variations.

Experiments.

The following pair of experiments was made under identical conditions:—

Table VI.

Experiment.	Nerve.	Anelectrotonus mean.	Neg. var. mean.	Katelectro. mean.	Inj. cur.	Notes.
728 VIII ..	Median (branch of)	0·702	0·356	0·595	0·20	Fig. 8
729A VIII	Splenic	0	0·540	0	0·80	Fig. 9

* Waller, 'Brain,' vol. 18, 1895, p. 210.

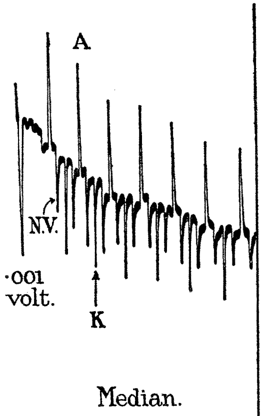

Fig. 8.—Exp. 728, VIII. Anelectrotonic and Katelectrotonic Currents, and Negative Variation on Medullated Nerve.

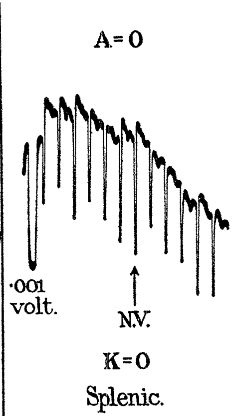

Fig. 9.—Exp. 729, A, VIII. The same on Non-medullated Nerve. An. and kat. are too small to be legible, and the negative variation only is seen.

The voltage of the polarising current was $\frac{2}{3}$ volt, the excitation 3000 units of the Berne coil, the distance between the centre of each electrode and the next was 11 mm.

In the medullated nerve the electrotonic currents exceeded the negative variation; in the non-medullated they were so small as to be imperceptible on the photographic plate. In order to see whether the electrotonic currents were completely absent, or merely very small, further experiments were then made, using a higher voltage in the polarising circuit.

These measurements are uncertain, both from the difficulty of measuring such very small currents, and from the fact that the cessation of anelectrotonus and the commencement of katelectrotonus excite the nerve, and the resulting negative variation in the latter case is added to the katelectrotonic current, so that except in special cases (as in Experiment 731) the readings of the latter are too high. It is also not absolutely certain that current escape has not some share in the result, though as all these effects are abolished by crushing the nerve, and as the an- and katelectrotonic currents are not equal in magnitude, and not exactly proportional to the polarising current, it is probable that this error, if it exists, is a small one.

Bearing these reservations in mind, certain conclusions may be drawn from these experiments. The electrotonic currents in the non-medullated nerves are evidently very small, about one-fortieth of the same currents in medullated nerves. Further, while the an- and katelectrotonic currents in the latter are nearly equal (0·702 millivolt

Table VII.

Experiment.	Polarising current (volts)									
		0·66.	1.	1·3.	1·6.	2.	2·7.	3·2.	4.	Neg. var.
729, B. VIII	Electrotonic currents (millivolts) A K	? ?	0·035 0·088	0·044 0·11	0·053 0·11	0·066 0·080	0·088 0·080	0·11 0·088	0·17 0·12	0·651
	Polarising current (volts)	2.	3.	4.	4·8.	6.	Neg. var.		Fig. 10.	
730. VIII.........	Electrotonic currents (millivolts) A K	? ?	0·045 0·041	0·090 0·045	0·12 0·041	0·16 ?	0·506			
	Polarising current (volts)	2.	4.			6.				
731. VIII	Electrotonic currents (millivolts) A K	? A ? K	0·071 0·11 0·11 0·094 0·024 0·024 0·024	=0·096 (mean) =0·024 (mean)	.. ..	A = 0·12 K = 0·038	Later experiment with same nerve as 730, now giving no negative variation on excitation.			
	Polarising current (volts)	2.	4.	6.	8.	Neg. var.				
732. IX	Electrotonic currents (millivolts)	A = 0·02 K = 0·01	0·05 0·02	0·065 0·025	0·085 0·025	0·625				

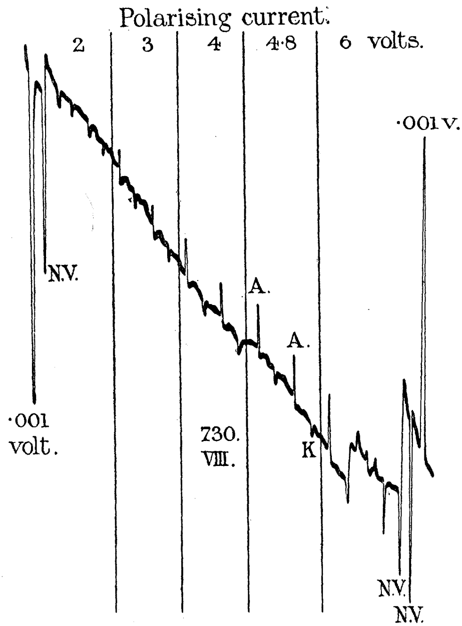

FIG. 10.—Exp. 730, VIII. A. and K. Currents only, with Increasing Strengths of Polarising Currents.

in A and 0·595 millivolt in K in Experiment 728), in the splenic nerves the anelectrotonic currents are perhaps four times greater than the katelectrotonic. This favours the view that these currents are not due to the presence of a small percentage of medullated fibres in these nerves, but are the actual expression of the fine sheaths present around the axis-cylinder.*

The result, therefore, of this series of experiments affords a very probable explanation of the diminution of the negative variation with successive excitations in the non-medullated nerve, and the relative absence of this diminution in the medullated. For in the latter the exciting current can diffuse up and down the nerve, in the former it is strictly limited to the spot where it is applied, and the current density at the excitable axis-cylinder must be many times greater in the non-medullated nerve. It is not surprising, therefore, that there should be a marked local effect, and whether this is termed "injury" or "fatigue" is rather a question of terminology than of fact.

* Dr. W. M. Fletcher has recently examined the sheaths of medullated and non-medullated fibres between crossed nicols. He finds that in the former there is characteristically present an anisotropic cholesterin deposit; in the latter this is absent. The sheath round the non-medullated axis-cylinder is therefore of a totally different character to that in the medullated fibre. (Note communicated to the writer.) See also authors quoted by Brodie and Halliburton, *loc. cit.*

As the electrotonic currents are so small, it was not to be expected that there should be any marked alteration of excitability in the neighbourhood of the kathode or anode of a constant current. Three experiments were, however, made to serve as a check on the preceding:—

Table VIII.

Experiment.	Neg. var. (mean). Initial.	Neg. var. (mean). during anelec.	Neg. var. (mean) during katelec.	Neg. var. (mean). Final.	Notes.
743, X. Polarising current = 0·5 volt. Excitation = 1000.	0·488	0·468	0·452	0·460	
744, X. Polarising current = 2 volts.	0·492	0·453	0·444	0·434	Same nerve as 743.
745, X. Polarising current = 2 volts.	0·971	0·931	0·928	0·884	

The exciting electrodes were at a distance of 3 mm. from the polarising, and on their distal side. From an inspection of the figures it is clear that even taking the most favourable case of the last experiment the effect is a minimal one.

I have much pleasure in acknowledging the kind assistance and advice I have received from Dr. Waller in the prosecution of this research, and also in expressing my indebtedness to the Council of the Zoological Society and Dr. Chalmers Mitchell for permission to use the nerves of the horses which had been slaughtered for the carnivora.

Conclusions.

1. Non-medullated nerves exhibit a negative variation and current of injury of about three times the magnitude of the similar phenomena in the medullated nerves of the same animal.

2. The negative variation of non-medullated nerves undergoes a progressive diminution with repeated stimuli.

3. The immediate cause of this diminution is a localised change at the place of excitation.

4. The electrotonic currents of non-medullated nerves are very small, about one-fortieth of those in medullated nerves.

5. This latter fact affords an explanation of 2 and 3, as the exciting current, being confined to the place of application, has a greater current density and therefore a greater local effect.